The 1 Mol Mescaline Adventure: A High-Yielding Synthesis from 3,4,5 – TMBA to Mescaline HCl

Preface:
Here is a standard run with the latest(-ish) techniques, utilizing 2-HEAA as the catalyst in the Henry Reaction in the first part, and a $NaBH_4$ + $CuCl_2$ reduction in the second. This time the synthesis was monitored with TLC (thin-layer chromatography). This is pretty much the same as the 2C-B write-up up to 2C-H, but now the scale is larger, and the yields even better.

One can also consult this guide when out to make 2C-H, 2C-E from 2C-E benzaldehyde, amphetamine from P2NP, etc…

We really need more Mescaline in the world and it is really not all too difficult to make, so let's get cracking.

Chem info:
3,4,5-Trimethoxybenzaldehyde ($C_{10}H_{12}O_4$, 3,4,5-TMBA) Molecular Weight (M.W.): **196.2 g/ mol**, white to slightly yellow solid, flakes. Slightly soluble in water, IPA, MeOH (wiki states in MeOH: 0.1g/ mL). Melting Point: 73 °C

3,4,5-Trimethoxy-β-nitrostyrene ($C_{11}H_{13}NO_5$, 1,2,3-Trimethoxy-5-[(E)-2-nitroethenyl]benzene, 3,4,5-TMNS) M.W. **239.225 g/ mol**, bright yellow solid needles or fine powder. Not at all soluble in room temp. water, not very soluble in room temp IPA, methanol (MeOH). Melting Point: 72 - 73 °C

Nitromethane (CH_3NO_2, NM) M.W. **61.04 g/ mol**, density: 1.1371 g/ cm^3, slightly fruity smelling clear liquid. Boiling Point: 101.2 °C
Ethanolamine (C_2H_7NO, monoethanolamine, MEA) M.W. **61.084 g/ mol**, density: 1.0117 g/ cm^3, viscous colourless liquid with an ammoniacal waft, might fume a bit. Boiling Point: 170 °C
Acetic acid (CH_3COOH, AcOH, glacial acetic acid or GAA) M.W. **60.052 g/ mol**, density of liquid form: 1.049 g/cm^3, heavy vinegar smell. Melting Point: 16 to 17 °C, Boiling Point: 118 – 119 °C
Isopropyl alcohol (IPA) Density: 0.786 g/cm^3, Boiling Point: 82.6 °C

Optional: To use as the TLC eluent we need hexane and ethyl acetate (EtOAc)

Part 1:
Synthesis of 3,4,5-TMNS (3,4,5-trimethoxy-beta-nitrostyrene) from 3,4,5-TMBA (3,4,5-trimethoxybenzaldehyde), scale of 250 g / ~1.3 mol+ (The Pretty Bit, Henry Reaction)

1) Start with **250.68 g TMBA or 1.277 mol**. Suspend/ dissolve this in **7x IPA or 1760 mL IPA**. Use a 5 L beaker with magnetic stirring on a hotplate. Most likely everything will not dissolve at this point.

Previously I ran the reaction without IPA in an excess of AcOH + NM, but the reaction occurs too quickly and everything turns into a thick paste/ mush, I believe it would not go to completion and no crystals would form as well. Possibly lots of unreacted TMBA was trapped in the porridge.
It seems that with IPA it takes longer to react, but the mixture does not seize up and the product crystallizes beautifully as the reaction mixture cools. Yields are satisfactory using IPA as well.

2) Prepare a **15% mol. eq. of 2-HEAA** (2-Hydroxyethylammonium acetate) in a separate beaker. Or 0.19155 mol MEA or 11.7 g or **11.56 mL** with a bit more **AcOH**, 0.192 mol or ~**11 mL**. In a beaker pour acetic acid onto MEA, the mixture heats up quite a bit, smoke is released, and it becomes much thicker and more viscous. You could just pour the ethanolamine straight into reaction mixture, but it really does release a lot of heat, so probably illogically I do this separate and wait for it to cool to "protect" the TMBA. As well you can suck away the fumes easier.

Later, during the course of the reaction I decide to pour an **additional 50 mL MEA** straight into into the reaction mixture as it seemed the reaction was going slow, so a 15% mol. eq. might not be enough.

3) In total will use a 2x mol amount of AcOH (an excess). Or 2.554 mol. Already used 0.192 mol making the 2-HEAA, so 2.362 or ~**135 mL additional acetic acid**. However, later on I add 300 mL more AcOH to help dissolve the benzaldehyde. So just use as much to make sure the benzaldehyde *just dissolves with mild heating*. That way when the mixture cools after you have decided the reaction is over, crystals will crash out and grow in the beaker.

4) Use a 1.05 mol. eq. or 1.34085 mol or 81.845 g or ~**72 mL** of NM. Reaction starts to proceed slowly at this point, so we need a catalyst. But before adding the 2-HEAA (or straight MEA), make sure the 3,4,5-TMBA is fully dissolved and the liquid is clear (maybe a light yellow). Heating will help to dissolve.

5) Add in the 2-HEAA and still some of the benzaldehyde is not dissolved, so add 80 mL NM, helps to finally fully dissolve the substrate.

6) Will be running the reaction monitoring on TLC plates. After some experimentation I figure out that a **6:2 hexane: EtoAc mixture is ideal as an eluent**. But mix 6.5 mL n-hexane with 2 mL EtoAc by error. A 250 mL beaker was the developing chamber for cheap **25 x 75 mm** sized TLC plates from AliExpress. **GF254** type **silica gel.**

Beforehand, **50 mg** of the benzaldehyde was dissolved in **2 mL IPA** and kept in a glass vial. This was the benzaldehyde standard (labelled as *Be* on the plates).

Run TLC on the first plate 35 min after the addition of the 2-HEAA in hopes of seeing something unexpected. The reaction mixture I draw with a regular pipette and dilute one drop with 0.5 mL fresh IPA. To spot on the TLC plates used a micropipette and 1.5 µL drops. *Rx* (reaction) and *Co* (combined spot) were about the same as the *Be* control. Spots maybe a bit large.

7) After 1 h 25 min add the additional **50 mL MEA**, as the reaction seemed to be going slow, don't think it changed much. There is significant colour change at this point, and the liquid is turning more and more yellow. Smoke or some sort of mist forms on the surface of the reaction mixture after addition of MEA, suck it away.

8) Take TLC after 1 h 45 min and it does seem to show two spots with some sort of product, a tail above the 3,4,5-TMBA, but there is clearly lots of unreacted BA left. Heating contines…

9) … and take another plate after 2 h 30 min, but to mix things up I decide to try a different eluent, Make one with 5 mL DCM and 0.2 mL MeOH. The DCM pulls the *Be* spot too high, This eluent mixture was more polar than hexane and ethyl acetate one.

10) After 3h TLC shows that much 3,4,5-TMBA remains, so at 3 h 20 min add **30 mL more NM**.

11) Made a few more TLC plates and finally after about **7 hours of the reaction** running between 50 – 60 °C but mostly at **55 °C**, with gentle magnetic stirring, TLC shows only the faintest or no 3,4,5-TMBA spot. At this point the colour change of the liquid had gone from a yellow, to a darker yellow, to an orange then all the way to a dark ruby red. The colour also seems to be a good indicator of when all of the 3,4,5 – TMBA has reacted, in these conditions look out for a dark blood ruby red but not blackish colour.

12) Once removed from heat, stirring stopped, crystals grow fairly quickly and within an hour the beaker is full of **yellow needles**. Leave to sit at room temp. overnight.

Now be careful working with the formed nitrostyrene, it is an irritant, and will especially make you sneeze and wheeze. Makes your nose runny, so in general wear a mask when really digging into it.

13) Vacuum filter and set aside the mother liquor to freeze in the freezer to collect a second crop.

14) While still in the Büchner funnel, wash with room temp dH_2O. **Wash** with a large amount, maybe **700 mL, let the crystals sit and fully soak** in the water as well. There is no harm done, they do not dissolve in water. Make sure no smell of AcOH remains, this is what I want to avoid, in the next step water or IPA is no big deal as that is where the reaction will take place, but AcOH is something to avoid. As well AcOH is hard to evaporate and smells bad. That is another advantage of using more IPA in the procedure.

No need to wash with any 10% sodium bisulfite sol. as TLC showed no benzaldehyde remained.

15) Take TLC of the final product. The control *Be* or BA (benzaldehyde) lane has an $\mathbf{R}_f$ of 0.5 (eluent front travelled 6.1 cm while the spot travelled 3.05), while the NS (nitrostyrene) lane has a slightly higher $\mathbf{R}_f$ of 0.56. The spot is slightly yellow as the product is yellow. In the Co (combined) lane, there is a NS hat on the BA. Only one spot of nitrostyrene in the NS lane, product seems to be pure, the reaction is a success.

During the course of the reaction, monitoring on TLC, you will see that the hat (nitrostyrene product) will become brighter and the head (3,4,5- TMBA) will fade.

16) From the freezer collect the second crop of crystals. Some more have fallen out, but it is a different colour, bit more greenish-yellow and darker, but they might be more dense. For some reason wash with 10% sodium bisulfite sol. to see what happens, no adduct is formed. Then wash with water.

17) Take TLC of the reaction mixture, and it also shows something similar to nitrostyrene, meaning there should be more product dissolved to collect, but somewhere along the line I forget to dump cold water into the final reaction mixture. The liquid was still a dark red, adding water should have precipitated more crystals. But had dumped out the reaction mixture already.

18) Fully fan dry both crops, the second crop I could have washed with water a bit more as there was a slight

odour of acetic acid. Drying does not present a problem and have a fine yellow powder from the first and a more green denser powder from the second crop. Both look very good.

19) I do not recrystallize the batch. There is no benzaldehyde in there, it is dry and looks very clean, don't see a reason to use litres and litres of MeOH in an arduous Re-x and then loose half the product. This turns out to be the correct decision. In the following reaction I still get a good yield, so a re-x is not a prerequisite in this synthesis. It can be skipped if your product is obviously clean.

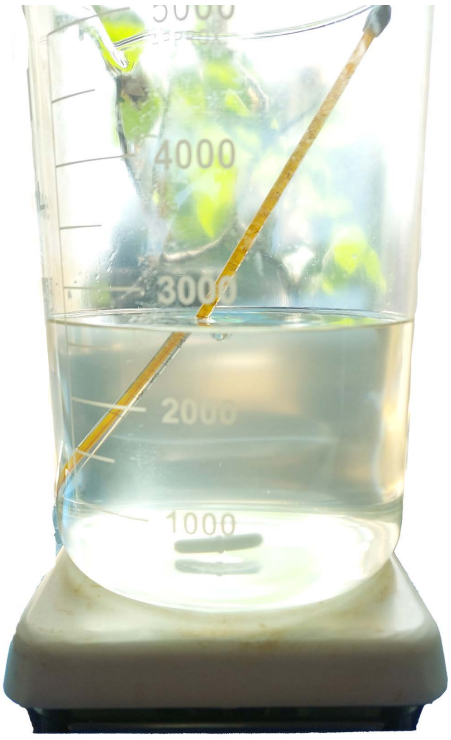
Yield is 207.26 g from the first crop, 30.74 g from the second. A combined **238 g or 0.995 mol.** This is a **75% yield**. Would certainly have been higher if I collected a third crop.

Findings and Observations:
To compare, 3,4,5-TMBA is much slower to react than 2,5-DMB. The reaction took about 7 hours in these conditions. The total amount of liquid to dissolve the benzaldehyde just above room temp was about **7.85x** its weight. One improvement could be to speed up the reaction, using more heat might help in this case but in general ethanolamine in IPA works well and in pretty good yields to make Mescaline nitrostyrene

As well, monitoring with TLC helped so much to know what was going on and what decisions to make. Now I know a whole bunch, and now you know. And now I know that if you have some bomb ass looking nitrostyrene then a recrystallization will be a waste of time and nerves. Go ahead and just dump it onto the $NaBH_4$ like we are about to do in the next step.

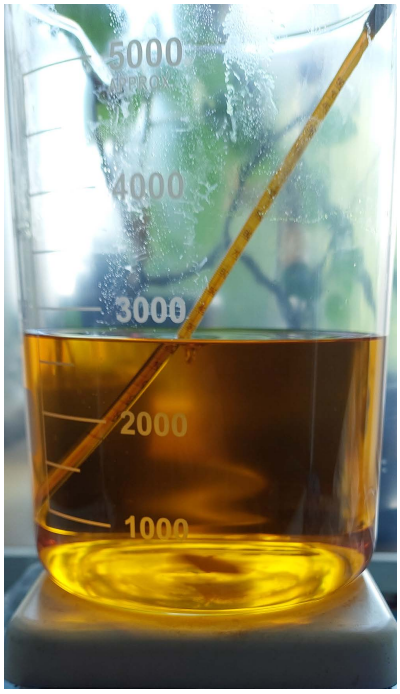
This link might help as well:
https://www.sciencemadness.org/whisper/viewthread.php?tid=157292&page=2

A few images to savour for Part 1:



Dissolved benzaldehyde before addition of 2-HEAA

Colour 30 min after addition



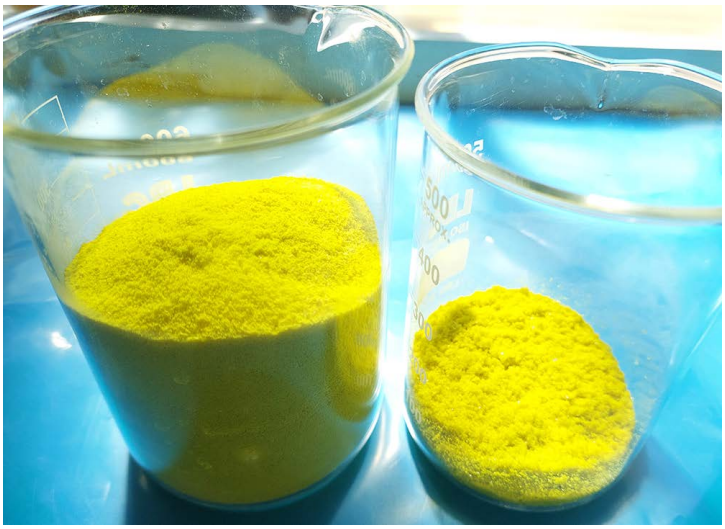
Colour darkens as reaction proceeds

Mixture colour towards the end

Crystals begin to grow when removed from heat

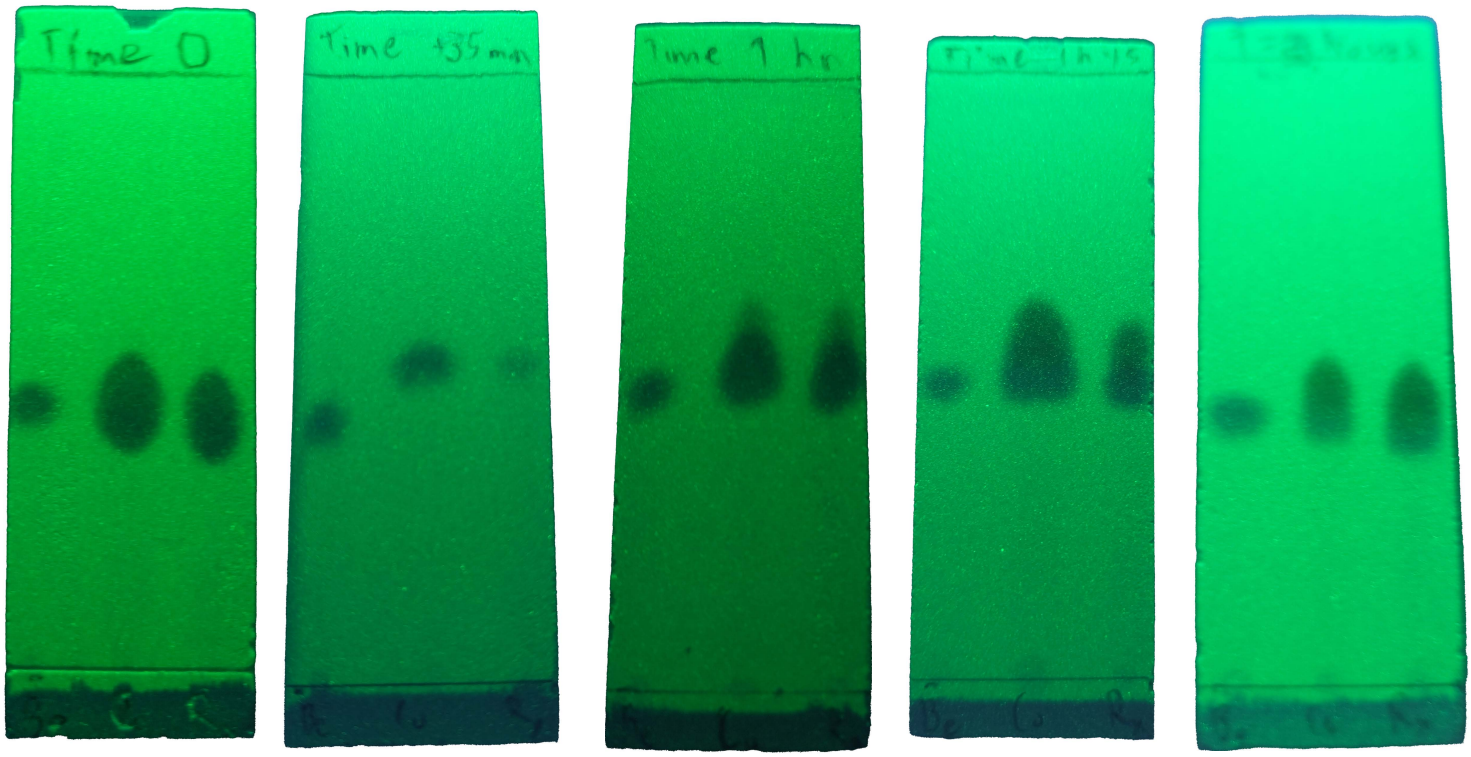
Crystals forming

Washing the nitrostyrene with water

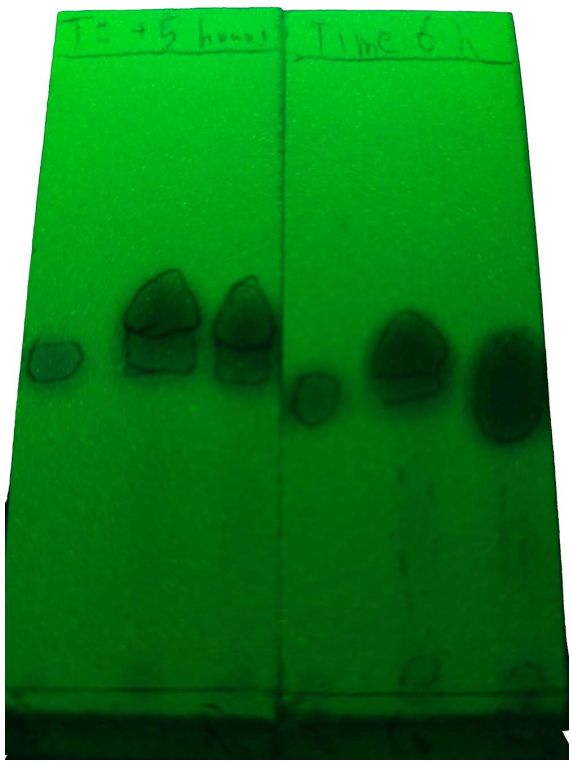


Final dry 3,4,5-TMNS

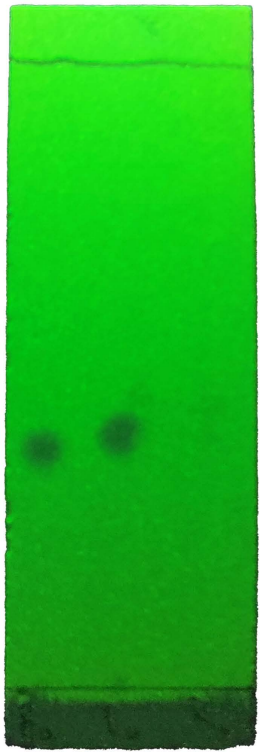
A Fine Selection of TLC Plates for Part 1:



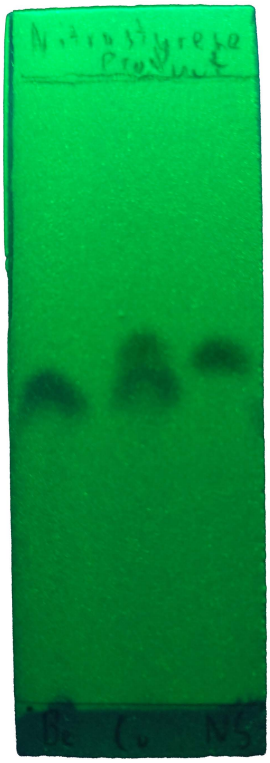
On the left is the benzaldehyde control, middle is Co spot, right is reaction. From before catalyst addition to 3 hours.



Hours, 5 and 6, but hour 6 Rx is too concentrated, spot is too large.



Different eleunt NS on the bottom, didn't move. No 3,4,5-TMBA remains. Possibly hour 7.



Test of the final product, one spot

Part 2 of The 1 Mol Mescaline Adventure: Reduction of Mescaline nitrostyrene (3,4,5 – TMNS), to Mescaline freebase with Sodium Borohydride and Copper(II) chloride

Preface:

We continue on our merry way, and now we will reduce the nitrostyrene to 3,4,5-Trimethoxynitroethane with sodium borohydride ($NaBH_4$), then addition of $CuCl_2$ will hydrogenate the nitroethane to form mescaline. As I understand this is roughly what occurs. Scouring older write-ups I notice that for the reduction, a 4 mol. eq. was generally used. We use in total about a 7.5x mol. eq. the extra 3.5 mol of boro is used to create a massive amount of Hydrogen gas when the copper eats very quickly and violently into it. Now I am not certain if a total of 7.5x mol eq. of borohydride are really required. In any case I tend to use a bit less.

Otherwise, as recently with 2C-H, use a **1.3:1 IPA: dH_2O mix** as the reaction medium. The increased water proportion seems to work well with 3,4,5-TMNS as well. Used 12x the liquid amount as the NS, but I notice that this could also be reduced, perhaps to **10x**.

Chem info:

Mescaline ($C_{11}H_{17}NO_3$, 2- (3,4,5-trimethoxyphenyl)ethanamine, 3,4,5-Trimethoxyphenethylamine, M)
M.W. **211.261 g/ mol** (freebase), 247.719 g/ mol (HCl salt), 278.316 g/ mol (hemisulfate dihydrate)
The sulfate (actually hemisulfate dihydrate or 1 molecule of mescaline per ½ H_2SO_4 with 1 molecule of water) appears as a fine white powder, while the HCl pure seemed to be crème coloured, slightly off white peachy.
Melting points: 35-36 °C (freebase), **181 °C** (HCl), **183 – 186 °C** (hemisulfate dihydrate) (from *Phenethylamine Von der Struktur zur Funktion* - Trachsel)
pKa: 9.56 (also from *Phenethylamine Von der Struktur zur Funktion* - Trachsel)
Sulfate salts I found to be only moderately soluble in room temp water. The freebase oil will pick up CO_2 from the air and form a carbonate salt.

Sodium Borohydride ($NaBH_4$) M.W: **37.83 g/ mol**, white powder/ crystals, hydroscopic, forms a cake exposed to air.
Copper (II) chloride dihydrate ($CuCl_2{\cdot}2H_2O$) M.W. **170.48 g/ mol**, green solid metal, somewhat soluble in IPA, more soluble in water. Metal spoons will rust instantly on contact.
Sulfuric acid (H_2SO_4) M.W. **98.079 g/ mol,** 1 litre of concentrated sulfuric acid (98.3%) contains 18.4 mol, colorless, transparent viscous liquid. Can be distilled from drain cleaner. Density: 1.8302 g/cm^3
Hydrochloric acid (HCl) M.W. **36.46 g/ mol**, 1 litre of concentrated aq. HCl (36%) contains 11.64 mol, colorless, transparent liquid that fumes when exposed to air. Density: 1.18 g/ cm^3
Sodium Hydroxide (lye, caustic soda, NaOH): M.W. **39.9971 g/mol**, white, opaque crystals
Dichloromethane (CH_2Cl_2, abbreviated as DCM): boiling point: 39.6 °C, density: 1.3266 g/ cm^3, colorless liquid, chloroform like smell but fainter.

Magnesium Sulfate ($MgSO_4$) and Potassium Carbonate (K_2CO_3) as drying agents, K_2CO_3 also helps to raise the pH and might thus quench the reaction.

Part 2:

1) Start with **238 g** from the two crops of 3,4,5-TMNS. Plan to add the first crop and then the second. But it didn't make a difference, both reacted the same. Second crop might have some very little acetic acid and that was I was a bit hesitant. Calculate as **0.995 mol.**

2) Try and use a **~12x liquid amount or 2.9 L**. Again use **1.3:1 IPA:dH_2O**. Use **1650 mL IPA** and **1250 mL water** that I pour into a **10 L three-neck round bottom ffask**.

As a rule of thumb, for this reaction involving copper chloride, you want to have at least **3x the size of the reaction ffask** to the liquid amount. So maybe you could get away with 325 g NS and 3.3 L liquid.

The middle neck is equipped with overhead stirring, with a side neck holding a thermometer, the third neck has a funnel for additions. Place the contraption into a 20 L bucket with ice-water. Use more crushed ice, less water. Wait for the internal temp to fall to about 10 °C or lower. Have about 4 - 5 kg ice on hand.

3) Calculate a **7.5 mol. eq. of $NaBH_4$** or 7.4625 mol or **282.3 g**. Round to 280 g. Use **230 g initially**, and plan to add **50 g before the addition of copper**. However, I now believe that only a 4x mol. eq. is required for the first part, or 150 g, then maybe add 50 g before the copper. This is after finding other reports.

Add the first half of the boro when the temps have dropped (won't react with water as much at lower temps) making sure it is finely crushed before pouring in.

4) Calculate $CuCl_2 \cdot 2H_2O$ amount. Use less this time as this is a bunch of copper already. Still more than the original Jademyr paper. Use a **17% mol. eq.** or 0.16915 mol. or **28.84 g copper chloride dissolved in 115 mL (1:1 IPA:dH_2O)**. Dissolve in 57 mL IPA + 57 mL dH2O. Takes a bit of crushing and stirring to fully dissolve. (4x liquid as copper). Would use even less copper next time.

Prepare everything and proceed to tango!

5) The internal temp only dropped to 12 °C, it was a very hot day, and I use too much water to ice. Add a few large spoonfuls of NS and temp rises to 16 °C. Continue adding nitrostyrene and loading more crushed ice into the bucket. Addition takes 2 h 25 min, but I was taking breaks. The way to do it, add 3 or so spoonfuls, temps rise, wait a bit for the reaction to subside add again. Max temp was 21, most addition took place at **18 °C**. Seems fine, the 3,4,5 – TMNS does not react that strongly.

6) After the last addition of the nitrostyrene, pour in the additional **40 g $NaBH_4$**. Believe that the boro does not dissolve. Colour of the mixture is milky white, not much colour remains. I do not monitor with TLC this part of the reaction as it should be visible when the yellow of the nitrostyrene has disappeared. The nitroethane is white.

7) Remove the bucket and spin at room temp for maybe 20 min. Prepare a TLC eluent with 6 mL hexane and 2 mL ethyl acetate. But it proves not to work, spots no longer work. A better eluent **is 98 parts DCM to 2 parts MeOH to 0.4 parts NH_3**. Try 5 mL DCM with a dash of IPA. Does not work well either. Finally the planned eluent of 5 mL DCM, 0.1 mL MeOH and 1 drop of 25% NH_3 proves to work. Spots move to roughly the center of the plates.

I believe I take a control NS lane just before the addition of copper.

8) Use a **100 mL pipette** to add the copper, position the open neck away from me, into an inline exhaust fan as there might be spitting and lots of gas evolution. As the mixture is spinning slowly, reach deep with the pipette just above the vortex centre, and squirt in as fast as possible. This does not prove to problematic either. Squirting with a pipette is slower than just pouring everything in at once from a beaker, and as well squirting just above the liquid helps with spitting and eruptions.

Turn off stirring quickly and place the flask into a **10 L heating mantle**.

9) Now I connect a large **600 mm bulb (Allihn) condenser** to one of the necks, which is cooled with water coming from a bucket. An aquarium pump in the bucket circulates the water.
However, I have an intuition that even this lightsaber is not powerful enough. So connect to the top another 400 mm bulb condenser, which is not cooled. Proves to be the correct decision, when stronger overhead stirring is applied in the beginning, so much hydrogen gas is evolved that it pushes the reaction mixture all the way up the first condenser and sometimes a little bit into the second one.

One truly giant metre long condenser would also work, but when carrying out a 500 g+ reaction in a 20 L flask, I would use 2 600 mm or 2 1000 mm condensers connected to separate necks. So maybe a reaction flask with 4 necks is better to use in that case.

This much copper eating away into the boro truly makes for an awe-inspiring or slightly disquieting spectacle. There will be a wind of hydrogen that blows into your room, and the whole vessel will sputter and gurgle as if a tubercular patient on their deathbed.
Remember, in the beginning stronger stirring is all that is needed to push the reaction mixture up to 70 °C, if the foam is nearing uncomfortably close to the top of the reaction vessel or IPA is about to be pushed out of the condenser, just turn off stirring. At this rate things quiet down after about 20 min.

10) Once the initial madness subsides turn on the heat and heat the mixture to **78 - 80 °C.** Reflux.

11) Take TLC at 45 min (showed most nitroethane had reacted, but a faint spot left), 1 h (wrong eluent), and at 1 h 15 min, can conclusively see that the conversion is fully complete. So once reflux begins, **1 hour is enough**. The reaction is over.

Might have taken TLC to check whether truly all of the nitrostyrene had been reduced.

Original paper from where this $NaBH_4$ + $CuCl_2$ method originated:
https://www.docdroid.net/CyL8RLd/thesis-pdf
Same author, recent paper:
https://www.sciencedirect.com/org/science/article/pii/S1860539725000040

Some older info:
https://www.erowid.org/archive/rhodium/chemistry/2cb.beaker.html
https://www.erowid.org/archive/rhodium/chemistry/345-meo-ns.html

A Few Images to Savour For Part 2:

Workplace and Rig for Reaction

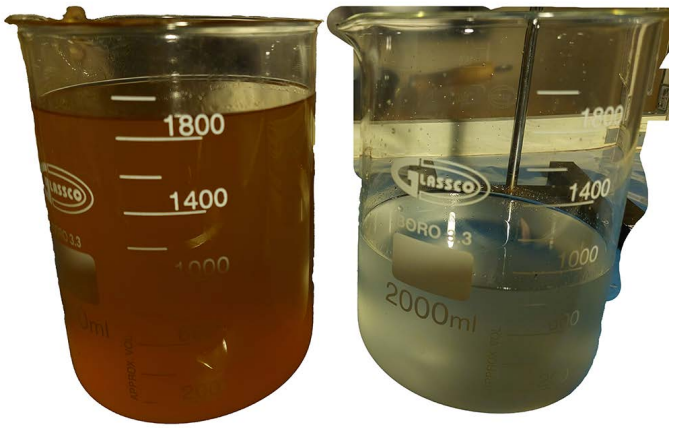
During nitrostyrene addition

Before addition of copper chloride

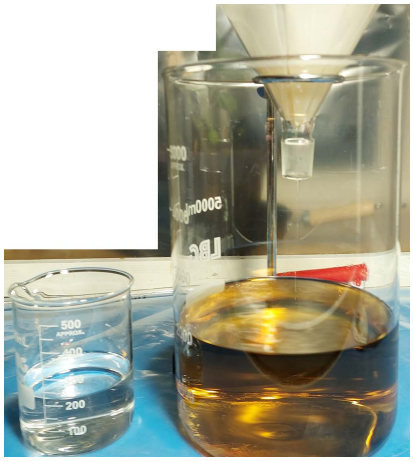
After addition of $CuCl_2$

Start of reflux, energetic, foaming, IPA rises high up the condenser

Pour into a 5 L beaker after reflux, mixture still hot



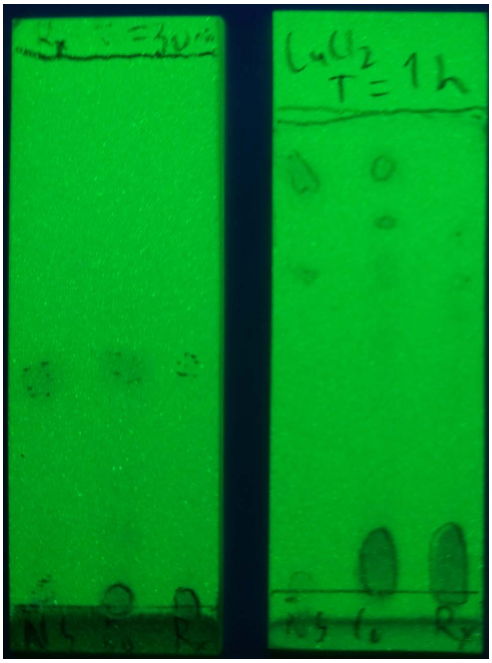
Copper filtered, layers separated. IPA layer on left, aq. layer to the right



Dilute sulfuric acid on left, dry and clear IPA layer on right

A Fine Selection of TLC Plates for Part 2:

Mystery selection, wrong eluent



Time 30 min, and 1 h, at 30 min, little NS actually nitroethane remains). Seems to be done at 1 h infact, wrong eluent

Better eluent, reaction most def done, mystery spot at top (maybe a stray)

Part 3:
Work-up of the reaction mixture. Filtration of copper nanoparticles, and separation of a clean IPA layer. Then salting with sulfuric acid, end up with a mescaline salt.

1) Now the following I do without a break all the way to a mescaline salt. With the reasoning that while the reaction is still hot or warm no borates will crash out, and it makes filtering easier as well. As the reaction mixture cools, the lower water one really thickens. And if you recall, the $NaBH_4$ was not fully dissolved when it was poured into the cold IPA + water. This also helps to use IPA + water in the first place.

Even when you have sequestered a clean IPA layer, it could be that leaving mescaline freebase out with impurities could lead to darkening and degradation. It is a lot of work for a single day, plan this run well.

Pour the hot mixture into a **5 L beaker**, wash the flask with 90 mL fresh IPA, add to the beaker. Decant most of the top cloudy golden IPA layer into another beaker being carefully not to pour any black copper floating on the bottom of the IPA layer.

2) Filter 3x until almost no black remains. This is probably overkill as there will be subsueqent filtration and separation steps that will get all of the copper out. Separate the layers with a 2 L sep. filter.

3) Most of the **product** should be **in the IPA** layer but decide to extract from the aq. as well. Extract with 190 mL, then 170 mL fresh IPA. Discard the aq. layer. Now have 2260 mL of the IPA layer to work with. Need to **dry it**.

4) Prepare **K_2CO_3 brine**. Will wash with a brine volume of **20% of the IPA** layer 2 times. So with ~450 mL each time. Prepare **460 g K_2CO_3 with 440 mL dH_2O**. Mixture heats up, take a break while it cools. Transfer to a large 5 L sep. funnel and wash twice with brine. Should have dried the IPA very well, and helped to quench if a reaction was still occurring. The brine would have pushed up the pH. However I am not sure if this is the appropriate brine amount to use.

5) Layer still cloudy. Maybe drying further with **$MgSO_4$** will help? Prepare 20 g $MgSO_4$, but with additions under stirring see that the $MgSO_4$ is not clumping, the layer is already dry. Not much $MgSO_4$ was needed. Layer is still cloudy.

6) Decide to filter under vacuum. Maybe then it will clear. Nope.

7) As a last resort, bring out my magic filter paper that I fan flute fold. Begin gravity filtering. It takes ages but I can see that it works! The layer is coming out clear! This is probably total overkill and a cloudy layer is just fine, but with a clear layer you buy yourself a front row seat to the spectacle of watching mescaline sulfate form. Up to you.
Am left with a beautiful golden IPA layer, not overly dark. This is the just the colour to look for. Light golden.

8) The layer is ready for H_2SO_4 at this point. Calculate the amount of sulfuric acid. As mescaline creates a hemisulfate, or **two molecules of mesc. bond to one H_2SO_4**, we only need half the mol. amount of H_2SO_4. I reason that an estimate of a 85% yield is a good starting place. So 0.846 mol, but half this amount, or 0.423 mol. 95% H_2SO_4 (stuff that I have) is roughly 18 mol/ L so need **~23.5 mL conc. sulfuric acid**. This I will **dilute in 235 mL IPA** (~10%).

9) Diluting sulfuric acid is not as simple as pouring in IPA straight. The mixture heats up, and if done too quickly the IPA boils and discolours.

So a **procedure for diluting sulfuric acid in IPA** would be:

- Place a 250 mL beaker into a bowl with ice water, fill with maybe 50 mL IPA
- Put on a mask and gloves
- Measure out your sulfuric acid and place into a separate beaker
- Using a pipette slowly squirt in the H_2SO_4, watch the IPA bubble, make sure it doesn't bubble too much, make sure the IPA does not change colour to yellow or red. If there is colour change, dump the IPA and start over
- Mix with a spoon wait a few moments and squirt some more H_2SO_4 in
- Once all the H_2SO_4 fill with IPA to the appropriate level

10) As the pKa of mesc freebase is 9.56 we should aim for a pH of 6.56, was using an incorrect source and actually aiming for 6.9 pH. Pour a portion (120 mL) of the IPA layer into a separate beaker in case I overshoot and add too much H_2SO_4.
As I pour in the dilute sulfuric acid, a white mass falls out straight away. Eventually the beaker is quite full and stirring is difficult, use a spoon. Once the pH nears 7.5 I take it very slow and start pouring in portions from the other beaker if it nears too close to 6.9. Eventually land almost dead on, at pH 6.85. But should have been aiming for **6.5 pH**.

11) Leave overnight (or early morning). Filter at the pump, wash with a large amount of cold EtOAc. The ethyl acetate does not wash any product away but it does help to clear the colour up. The product was already rather white and pure looking but after washing, end up with a bleach white paste that eventually dries to a fine talcum or baby powder just perfect for making your infant's butt white.

12) The mother liquor I set into a freezer, and eventually it seems that a bit more product ends on the bottom (but it might just have slipped past the filter). When I take it out of the freezer I had already made Mesc HCl, so just dump the mother liquor, there was not much there at all.

13) Fully dry, the butt powder weighs **211.784 g** or 0.761 mol of mescaline hemisulfate dihydrate. A **76.5% yield** from the nitrostyrene. Would say that this is a great result. 1 mol works just fine with the NaBH4 + $CuCl_2$ and if done right, the product out of the reaction is already very clean.

Findings and Observations:
So, a good yield even from un-recrystallized nitrostyrene, what do you know!
This sulfate you could consume as is, but I will do an A/B extract and convert to the stronger HCl which I believe to be superior. As well we will clean it further this way. This work-up is something that worked well. No need for an oxalate salt and no need to distill anything. No need to prepare dry HCl in IPA (but this might be a good option as well). Keep it simple. I would follow this procedure to form 2C-H hemisulfate, but keep in mind that 2,5-dimethoxynitrostyrene is more energetic compared to 3,4,5-TMNS when you are reducing it. More heat evolution, and much more foaming.

Part 4:
Acid/base extract and **conversion to the HCl salt**, clean with ethyl acetate. Grind into a fine powder.

1) Dump the mesc into a 5 L beaker, **suspend in 2 L dH_2O**. Start magnetic stirring. Don't expect the mesc to dissolve. In fact, maybe this was too much water.

2) Prepare a **20% NaOH sol.** Need a 1.05 mol. eq. or ~0.8 mol or **32 g NaOH in 160 mL dH_2O**. Wait for the lye water to cool, starting pH of the mesc suspension is 7.3. Keep on pouring and stirring and watch as the mesc dissolves with increasing pH. At **11.6 pH** all of the mesc is dissolved the layer is clear and light yellow. Used most of the prepared NaOH sol.

3) Transfer to a 5L sep. funnel the 2.5 L of liquid. **Extract with** 400, 300, 200 and 200 mL **DCM**.

4) Transfer the pooled DCM into a 2 L sep. funnel. Prepare 20% HCl. Need 0.77 mol, this works out to 60 mL 36% HCl, diluted in 350 mL dH_2O.

5) Now simply pour in the aq. HCl directly into the funnel. But pour a bit at a time, reacts quite strongly and heats up as well. A good procedure is to pour a few times, maybe swirl and then you need to cap the sep. funnel and shake strongly. JUST remember to vent, a lot of gas is produced. Shake just a bit and quickly vent at first, then later you can shake more.

As DCM and water do not mix well, you need to make sure to shake well. Don't worry, the DCM didn't form an emulsion.

6) Monitor pH and watch for it reach 6.5. I did this without leaving out a portion of the DCM and overshot the HCl addition, pH had dropped to 2 or 3, but don't think it is a big deal.

7) The DCM is yellow and the water layer is mostly clear, but discard the DCM layer. Turns out it is only a few impurities there. The water pour into a pyrex and on a hotplate with a fan blowing evaporate. This is a lot of water to evaporate, so maybe I could have diluted the HCl in even less water. Keep the hotplate at maybe 100 °C. As well it turns out that the mesc seems to liquify when it is hot, but that is actually more able to dissolve more mesc when hot, so just keep it on the plate for maybe 4 hours but still checking nothing burns.

8) Evaporate the last bit with a fan.

9) Grind the slightly off white chunks into a fine powder. Looks very good. Have **179.414 g** or 0.724 mol of the **HCl salt**, or a **95.2% conversion** from the hemisulfate.

10) Determine the melting point with a Thiele tube. Slowly heat with a camping stove light mineral oil in the tube. The sample melts between **180 – 184 °C** which corresponds to M. HCl.

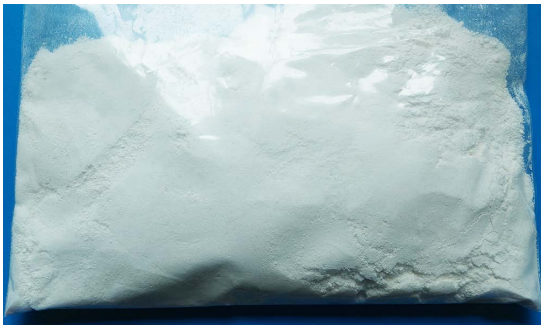
Job done. Now go out there and enjoy your medicine and enjoy the world.

Fin

Miscellaneous Imagery

Sulfate paste in a Büchner funnel after washing with EtOAc, unwashed was a bit yellow.

Dry sulfate powder



Bag of final HCl powder

Determining the compounds melting point witl a Thiele tube, sample unmelted in a capillary tube

Birch **Power**

frame for 5 L sep. funnel

Sample melted. Began melting at 180 °C, and was fully a liquid at about 183 or 184 °C